Application No.: 10/049,967 17790 (BOT)

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Exocytosis

AMENDMENTS

Amendments to the Claims

1-47. (Canceled)

48. (Currently amended) A method of treating a patient suffering from poisoning or at risk of poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of supplying administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient; a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor) to a cell of the patient, wherein the SNARE is resistant to proteolysis by the said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the elostridial toxin (toxin-inhibitory SNARE)

wherein the toxin-resistant SNAP-25 is a SNAP-25 resistant to proteolysis by the clostridial toxin;

wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin;

wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

49. (Canceled)

50. (Currently amended) A method of preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient; reversing the inhibition of exocytosis in a cell caused by contact of a clostridial toxin with the said cell, including the step of supplying a SNARE (soluble (N-ethylmaleimide-sensitive fusion protein)-attachment protein receptor) to the said cell not before contact of the said clostridial toxin with the said cell, wherein the SNARE is resistant to proteolysis by the

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said clostridial toxin (toxin-resistant SNARE) and/or is capable of inhibiting the clostridial toxin (toxin-inhibitory SNARE)

wherein the toxin-resistant SNAP-25 is a SNAP-25 resistant to proteolysis by the clostridial toxin;

wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin;

wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient at risk of poisoning when exposed to the clostridial toxin.

51-52. (Canceled)

- 53. (Currently amended) The A-method of either claim 48 or claim 50, as in any one of claims 48-50 wherein the said clostridial toxin is a botulinum toxin type A-(BoNT/A).
- 54. (Currently amended) The A method as in claim 51 of either claim 48 or claim 50, wherein the said clostridial toxin is botulinum toxin type C1-A (BoNT/A).
- 55. (Currently amended) The A-method as in claim 52 of either claim 48 or claim 50, wherein the said clostridial toxin is botulinum toxin type E-A (BoNT/A).
- 56. (Canceled)
- 57. (Currently amended) The A-method as in claim 54 of either claim 48 or claim 50, wherein the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 comprises a replacement of a said SNARE is a variant of SNAP-25 in which the residue equivalent to residue 197 and/or the residue equivalent to residue 198 of full length SNAP-25 are replaced by a residue other than Q-or a residue other than R, respectively.

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- 58. (Currently amended) The A-method as in claim 57 of either claim 48 or claim 50, wherein the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 comprises a replacement of a said SNARE is a variant of SNAP-25 in which the residue equivalent to residue 197 and/or the residue equivalent to residue 198 of full length SNAP-25 are replaced by a residue other than Q or a residue other than R, respectively.
- 59. (Currently amended) The A-method as in of claim 57, wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue other than R, selected from A, T, K, H or W and the residue equivalent to residue Q197 of full length SNAP-25 is Q or is replaced[[,]] by a residue selected from the group consisting of A, K-or and W.
- 60. (Currently amended) The A-method as in of claim 58, wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue other than R, selected from the group consisting of A, T, K, H-or and W-and the residue equivalent to residue Q197 of full length SNAP-25 is Q or is replaced, by A, K or W.
- 61. (Currently amended) The A-method of either claim 48 or claim 50, as in any one of claims 48-50 wherein the toxin-resistant SNAP-25 said SNARE that is resistant to proteolysis by the said clostridial toxin is capable of performing substantially the equivalent function of a SNAP-25 endogenously present in the patient to a SNARE present in the cell that is capable of being cleaved in the said cell by the said clostridial toxin.
- 62. (Currently amended) The A-method of either claim 48 or claim 50, as in claim 51 wherein the clostridial toxin poisoning is botulism said SNARE that is resistant to proteolysis by the said clostridial toxin is capable of performing substantially the equivalent function to a SNARE present in the cell that is capable of being cleaved in the said cell by the said clostridial toxin.

63-68. (Canceled)

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- 69. (Currently amended) The A-method of either claim 48 or claim 50, as in either of claims 48 or 49 wherein the patient is an infant.
- 70. (Currently amended) The A-method of either claim 48 or claim 50, as in claim 51 wherein the patient is an-infant adult.

71-72 (Canceled)

- 73. (Currently amended) The A-method of either claim 48 or claim 50, as in either of claims 48 or 49 further comprising the step of treating the patient with an inhibitor of the said clostridial toxin.
- 74. (Canceled)
- 75. (Currently amended) The A-method of claim 73, as in claim 73 wherein the clostridial toxin inhibitor is N-acetyl-CRATML-carcoximide of the said clostridial toxin is a SNARE that is capable of inhibiting the said clostridial toxin (toxin-inhibitory SNARE) or a recombinant polynucleotide capable of expressing the said toxin-inhibitory SNARE.

76-103. (Canceled)